STATE OF WASHINGTON
DEPARTMENT OF HEALTH
Office of Laboratory Quality Assurance
1610 N.E. 150th Street
Seattle, Washington 98155-9701

DATE: October 9, 2000

TO: Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

FROM: Gail V. Neuenschwander, Program Manager
Washington State Department of Health
Office of Laboratory Quality Assurance
1610 NE 150th St.
Seattle, Washington 98155

RE: Comments on Docket No. 00N-1394

---

1. Criteria used to demonstrate that a test is a simple laboratory examination with "an insignificant risk of an erroneous result".
   - The test should demonstrate no significant inaccuracy and no significant imprecision (CDC criteria) when tested by untrained users;
   - Waived tests run by untrained users should be compared with tests run in certified labs by trained personnel. As long as the test result is being used in the same manner by the clinician, there should be no difference in the threshold of performance.
   - **The model should also include the criteria that the test must pose no reasonable risk of harm to the patient if performed incorrectly**. Certain analytes (e.g. glucose, prothrombin time) should not be considered for waived status because the risk of harm is too high if the test result is inaccurate.

2. Criteria to determine if a methodology is "so simple and accurate to render the likelihood of erroneous results by the user negligible".
   - Since the test can be performed by personnel that are untrained in laboratory procedures and do not have the necessary knowledge to judge when the testing system is not working properly, the system must be failsafe or foolproof to not allow a test result that could be inaccurate. This would

require validation of the manufacturer's data in a setting using untrained users. The test results should be accurate at least 95% of the time.

- Certainly the accuracy becomes less important if the test does not have any major clinical impact, but then the question arises of why the test is being performed, and why is the test available on the market if it can not demonstrate accurate test results. The patient is certainly expecting a valid test result, and has no idea that the test might have only 75% sensitivity or specificity and could be performed by untrained laboratory personnel, with no oversight of the testing.

- One of the reasons that CLIA came into being was so that we could go to any laboratory, be it the hospital or POL, and get the same accuracy of testing. If the accuracy of the test is not considered when a test is approved as waived, we will be back where we started prior to CLIA. This is already true with many of the tests that have already been granted waived status.

- Laboratorians and other scientists will have widely varying opinions about what should be done to demonstrate "accuracy" (comparison to well-characterized reference methods or some other criteria). The accuracy of the test should be tested using untrained users, and the manufacturer's data should be validated to some degree. Regardless of the criteria, a reasonable degree of accuracy must be expected for all waived tests prior to market release. But "accuracy" must also be put into perspective with clinical usefulness. Clinical requirements for accuracy will differ, depending on the test (glucose, prothrombin time vs. urine dipstick, fecal occult blood), the setting (intensive care ward, physician's office, health fair) and the intended use of the test result (screening vs. diagnosis vs. adjustment of medication dosage).

- An area of major concern is the number of tests that are being waived simply because they can be sold over-the-counter (OTC). Many manufacturers are placing new tests in that OTC category simply because it doesn't require that the consumer be subject to QC requirements. It should not be allowed to be waived simply because it gets OTC status. These tests basically have no safeguards built in, as there are no QC requirements.

  There is a very different expectation of accuracy when a test is performed at home by a patient and when it is performed in a professional setting, particularly when the patient is paying for a professional result. If tests are used in the professional setting, they must meet more stringent accuracy requirements than those approved for patient self-testing.

  In the many years we have surveyed laboratories we have encountered situations where personnel with no laboratory training perform "simple" tests such as glucose on meters that are approved by FDA for home use. There have been many instances where the devices were not checked with quality

control material to ensure that they were working properly. There were also many instances when the devices were checked with quality control material and the results showed that something was wrong, yet the patient tests were still performed on the instrument and no investigative action was done to see what was wrong with the procedure. The nonlaboratorians performing the test expected that if the device gave an answer, it must be working properly.

3. Criteria used to determine that a test will "pose no unreasonable risk to the patient if performed incorrectly".
   - From our experience of looking at regulated labs that theoretically know something about QC and QA, we have seen circumstance where there is potentially great harm that can be done to patients with waived tests. Many times when labs are asked if they are running controls for their waived prothrombin times, glucoses, and lipid panels they are not even aware that there is quality control available because their "rep never explained that to them". Recently reviewing some proficiency testing that one of our labs was taking for their waived prothrombin time test showed that they had gotten a high prothrombin time result in seconds, but when they calculated the INR, which is what gets reported to the doctor, they reported it out as a normal INR. Even after they had been running this test for quite some time, being untrained laboratory personnel, they did not realize that this was an erroneous result. If this had been a patient, it could have had serious consequences.

   - The consequences of an erroneous result should be considered when granting waived status to any test by getting input from laboratory experts, clinicians and patients.

4. Screening tests that require a second test for confirmation.
   - It would be difficult to ensure that a confirmatory test would be done in each case, since there is no oversight of labs only performing waived testing. If the thresholds were to be lowered for these tests, it would be of utmost importance that the manufacturers label such tests in **LARGE BOLD PRINT** that a confirmatory test is mandatory, and that this information must be relayed to the patient as well.

   - Many people equate a waived test with a highly accurate test since it "poses no unreasonable risk of harm to the patient". In many cases manufacturers will have different versions of a test and when asked will say that the waived test is not their most sensitive or specific assay. The regulated versions of these tests require a few more testing steps, which increases the sensitivity and specificity. A test that gives false positive or negative results, or an erroneous result because it needs to be so simple to get waived status, certainly isn't serving the patients' well being. It potentially also increases healthcare costs to Medicare, the patient, or insurance company for a test that has little or negative value to the patient and may need to be repeated by a more accurate

method. If you had to chose between a test that was only 50% accurate and one that was 90% accurate, which one would you want to pay for or use to diagnose your illness?

General comments

The CLIA law states that tests, which are to be categorized as, waived are simple laboratory examinations and procedures, which have an insignificant risk of an erroneous result including tests:

- Approved by FDA for home use;
- Employ methodologies that are so simple and accurate as to render the likelihood of erroneous results negligible; or
- Pose no reasonable risk of harm to the patient if performed incorrectly.

Concern arises when a test is classified as waived based on **only one** of the criteria above, without taking into consideration the risk of harm to the patient if performed incorrectly. Since there are no personnel requirements for persons performing waived tests they can be performed by someone with no clinical laboratory training. If a test is performed incorrectly for such analytes as glucose or prothrombin time (both with methods that are currently waived) the risk of harm is immense.

How many true patient outcome studies have been done to demonstrate whether the "likelihood of erroneous results is negligible" for a particular waived test device? Who has demonstrated how often patients get the correct diagnosis or obtain appropriate treatment when testing is performed with a waived test device? Who has demonstrated how often patients are misdiagnosed or obtain inappropriate treatment?

How much does the clinical environment contribute to the usefulness of the test result and overcome any shortcomings in meeting some arbitrary "accuracy" limits or agreement with a "well-characterized reference method"? When waived testing is done in conjunction with the patient's visit, the patient and the clinician do have the unique ability to judge the reliability of the results that traditional laboratories do not have. Does that capability outweigh the need for overly strict accuracy requirements when used in that setting? For example, what would the accuracy expectations be for a prothrombin time result, where the patient and clinician know the patient's coumadin dose, other medications, diet, and the range of values deemed appropriate for that patient, considering their unique diagnosis and history?

Patient outcome studies must be done. Without data on patient outcomes, it is difficult to determine whether the "likelihood of erroneous results" for a particular waived test device is negligible or not.